

## Hair Loss Prevention

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### BACKGROUND

My invention relates to preparations useful for maintaining normal, healthy hair bulb function, for preventing hair loss, and for medically treating androgenic alopecia and like dermatological diseases. I will first review pertinent hair biology, then discuss prior art teachings in the field, and then describe my invention.

#### Hair Biology

Hair bulbs are responsible for normal, healthy hair growth and retention. Hair bulbs are located in the skin, about 3/16 of an inch below the skin surface. They are located just above the fatty layer at the very lower most position of the skin.

The majority of facial and body hair growth is stimulated by androgens. However, the growth of scalp hair has been shown, in genetically programmed individuals, to be inhibited by 5 $\alpha$ -dihydrotestosterone ("DHT") in individuals who exhibit a hereditary pre-disposition to baldness. Ebling, Dermatol. Clin. S. 467 (1987); Lucky, 4 Biochem. Soc. Transc. 597 (1988); Brodland et al., 47 Cutis 173 (1991).

DHT is produced by reducing testosterone with a 5 $\alpha$ -reductase

enzyme. The phenotypic expression of baldness does not occur in the absence of testosterone. Androgenic alopecia or common baldness represents 99 percent of all cases of hair loss. Broadland, id.

5                   The mechanism through which androgens regulate the biology of hair is by modulating the hair growth cycle. Ebling, 4 Biochem. Soc. Trans. 597; Bergfield et al., 5 Dermatol. Clin. 491. The effect of DHT on hair growth appears to be related to local rather than systemic levels of the hormone. This is because the capacity of scalp skin from balding individuals to convert testosterone ("T") to DHT is greater than that observed in the scalp of non-balding individuals. Lucky, *supra*; Schweikert et al., 38 J. Clin. Endocrinol. Metab. 811.

10  
15                   To prevent hair loss, maintain the health of hair bulbs, or to treat baldness, several compositions are known in the art. We discuss them now.

#### Hair Loss Prevention

20                   Hair loss prevention preparations are known in the art. These include natural product preparations, biological products, vascular toners and testosterone blockers. Several prior art compositions are discussed in the accompanying

Petition To Make Special and its accompanying references, the contents of which are incorporated herein by reference.

Natural Products. Several inventors disclose natural compositions. Casero, United States Letter Patent No. 5,340,579, discloses a composition comprising (a) mucopolysaccharides, (b) human umbilical cord extract, (c) tetrahydrofurfuryl nicotinate, and (d) pharmaceutically and cosmetically acceptable excipients. Buck, United States Letter Patent No. 5,512,275 and 5,609,858, discloses a formulation for the treatment of androgenic alopecia, comprising liquor carbonis detergens in combination with spirits of camphor, castor oil, isopropyl alcohol. Chizick et al., United States Letter Patent No. 5,972,345, discloses a combination of saw palmetto extract, African pygeum extract, and stinging nettle extract.

Biological Products. Hoke, United States Letter Patent No. 5,994,319, discloses using genetic material as a anti alopecia therapeutic. Hoke proposes using anti-sense oligonucleotides targeting 5- $\alpha$  reductases in conjunction with other hair growth enhancers. Tien, United States Letter Patent No. 5,574,011, discloses the use of a class of LHRH analogs for treating male pattern baldness. Messenger, United States Letter Patent No. 6,020,327, discloses administering aromatase inhibitors to treat hair loss. Liao

et al., United States Letter Patent No. 5,422,371 and  
5,605,929, discloses a class of anti-androgenic compounds.

Vascular Toners. Several organic chemicals are  
known to affect the hair growth and hair retention cycle.  
5 These include minoxidil. I refer to minoxidil and similar  
kinds of compounds as "vascular toners," because they are  
believed to be effective due to their impact on local blood  
circulation.

10 Minoxidil has been shown to stimulate hair growth  
or inhibit the loss of hair in a number of patients beginning  
to develop androgenic alopecia. Minoxidil is the generic  
name for 6-(1-piperidinyl)-2, 4-pyrimidinediamine 3-oxide.  
Its preparation is disclosed in Anthony, W.C. et al., United  
States Letters Patent No. 3,382,247 (1968); McCall, J.M., et  
15 al., 40 J. Organic Chem. 3304 (1975); Gorecki, D.K.J., 17  
Analytical Profiles of Drug Substances 185 (Academic Press,  
New York 1988). It is more soluble (by weight minoxidil /  
volume of solvent) in non-polar solvents than polar ones (75  
mg/ml in propylene glycol; 44 mg/ml in methanol; 6.5 in  
20 dimethyl sulfoxide; 2.2 mg/ml water).

Minoxidil is medically classified as an anti-  
hypertensive. It affects heart rate and rhythm. It has thus  
been used in an oral formulation as a cardiac drug.  
Andersson, O., 205 Acta Med. Scand. 213 (1979); Moser, M., 26

Advan. Cardiol. 38 (1979). Over dosage may create cardiac arrhythmias or other adverse side effects. See e.g., Carlson, E.S., 39 Toxicol. Applied Pharmacol. 1 (1977).

5 Minoxidil is also medically classified as an anti-alopecia agent. Its efficacy in treating early male pattern baldness has been described in numerous published articles. E.g., Olsen, E.A. et al., 13 J. Am. Acad. Dermatol. 185 (1985); Novak, E., 24 Int. J. Dermatol. 82 (1982). Its limited percutaneous absorption and secretion is described in Franz, J.T., 121 Arch. Dermatol. 203 (1985).  
10

The mechanism by which minoxidil alters the hair growth cycle is uncertain. It is thought to act by increasing vascular circulation to the hair follicle. It is known that minoxidil effectiveness is more pronounced in scalp areas which are more vascular.  
15

Topical minoxidil is know to have certain shortcomings. It is effective in only about eight percent of adult male users. It produces "lanugo," or baby-type, hair which is relatively thin. Further, and perhaps most significantly, after approximately 30 months of continuous use, minoxidil shows a sharp drop in effectiveness. After about thirty months of use, about half of the new hair growth falls out. Thus, while the user has somewhat more hair than originally, the user has less hair than originally seen.  
20

Testosterone Inhibitors. Inhibitors of steroid metabolism, particularly those that inhibit the conversion of testosterone to dihydro testosterone, have shown effects on hair cycles, including inhibition of hair loss. One class of enzymes targeted by these inhibitors are the steroid 5- $\alpha$  reductases.

Certain 5 $\alpha$ -reductase inhibitors have been shown to inhibit hair loss. For example, stump-tail macaque monkeys treated with the 5 $\alpha$ -reductase inhibitor 17b-N,N,-dimethylcarbamoyl- 4-methyl- 4-aza- 5 $\alpha$ -androstan- 3-one undergo significantly less age related hair loss than untreated monkeys. Rittmaster et al., 65 J. Clin. Endocrinol. Metab. 188 (1987). Similarly, finasteride, a 5 $\alpha$ -reductase inhibitor, miniaturizes scalp hair follicles, reversing the balding process. "Merck's Propecia Shows Promise In Hair Loss," Marketletter (Mar. 31, 1997). These inhibitors are thought to work by inhibiting the reduction of testosterone to DHT, as DHT is considered to be the more active form. The use of a combination of finasteride and minoxidil demonstrated that, in combination, these two drugs increased the rate of hair growth when compared to either compound administered alone. Diani, 74 J. Clin. Endocrinol. Metabol. 345.

Minoxidil used in conjunction with effectors of steroid metabolism, leads to enhanced hair growth and decreased rates of hair loss.

Testosterone blockers are known in the art (I use  
5 the term "testosterone blocker" to denote a competitive  
antiandrogen which inhibits the binding of testosterone or  
DHT onto its cell surface binding site, rather than a  
compound which is used to inhibit the reduction of  
testosterone into DHT.). Also known is their use  
10 systemically (orally or intravenously). As systemic  
therapeutics, they are known in the art as having a key  
shortfall: their long term efficacy is compromised by their  
blocking of the androgenic feedback inhibition of  
gonadotropin secretion. This interference results in  
15 elevated gonadotropin secretion, which in turn increases  
testicular secretion of testosterone. The higher level of  
testosterone eventually overcomes the action of the  
antiandrogen. Liao, *supra*, at col. 3, lines 16-31.

Thus, what is needed in the art is a safe and  
20 effective way to maintain both the healthy function of hair  
bulbs, and the health of existing hair, that avoids the  
shortfalls seen in the prior art.

SUMMARY

I have invented a kind of hair loss prevention composition. My invention is a new combination of already known types of compounds. My invention can be used either  
5 cosmetically (to maintain healthy hair growth) or pharmaceutically (to treat a medical condition). It can be made using components already known in the art, allowing one to enjoy the predictability of use available with these old compounds. My invention is flexible enough, however, to also  
10 allow one to substitute newly-discovered compounds substantially equivalent to the already known compounds. Thus, my invention can be adapted to allow the user to use the safest, most effective components then available.

I have found that certain compounds have greatly  
15 improved effectiveness - achieving *ten times* the benefit, or an entire order of magnitude - if combined with a skin penetration enhancer. The penetration enhancer delivers these compounds to the hair bulb, where the compounds are most needed.

20 I have thus found that testosterone blockers, if applied topically (rather than systemically administered), are effective in preventing hair loss, and if used in conjunction with a dermal penetration enhancer. Such topical use avoids precipitating the systemic increase in



testosterone production seen with oral administration, by  
minimizing systemic interference with normal gonadotropin  
secretion. I have also found that vascular toners, if  
applied topically in conjunction with a dermal penetration  
enhancer, work much better.

#### DETAILED DESCRIPTION

My invention includes a skin penetration enhancer  
used together with a testosterone blocker or a vascular  
enhancer, or both. I first discuss each component  
individually, and then discuss the combinations of these  
components that I have found most acceptable.

##### Penetration Enhancers

You can use a variety of skin penetration enhancers  
to make compositions that work as I intend. Penetration  
enhancers and skin penetrating formulations are known in the  
art. These include the variety of formulations used from  
time to time for both psoriasis treatment pharmaceuticals,  
and psoriasis prevention nutritional supplements and  
cosmetics.

The penetration enhancer (or penetration agent)  
should be accepted for human use by relevant government  
agencies. Thus, dimethyl sulfoxide, while within the scope  
of the claims, is not a preferred penetration enhancer where

that compound is not approved for human topical use. The penetration enhancer should not chemically react with any other ingredient to impair or alter the composition's stability and shelf life. Thus, one should examine the possible reactivity of a given penetration enhancer with a given testosterone blocker or vascular toner.

The penetration agent should be cosmetically acceptable. Thus, while I have tested dimethyl acetate, I do not favor it. While it is within the scope of the claims, it is a weak penetration enhancer. Thus, one needs to use a lot of it. In these high amounts, it smells bad. In contrast, methyl acetate is odorless, and I have tested and found it acceptable.

Several inventors disclose liposome technology to deliver cosmetic and dermatology materials. See, for example, Lishko et al., United States Letter Patent No. 5,753,263, discloses using liposomes to selectively deliver a composition to hair follicles. Liposomes are made of fatty material, and are suitable for delivering homogenous types of materials. As such, it may be difficult for a liposome to in fact work with a combination of a polar compound (like a minoxidil vascular toner) and a non-polar compound (such as a progesterone testosterone blocker). I thus do not consider

liposome technology within the scope of the term "penetration enhancer" in this patent.

#### Vascular Toners

5 My invention works with a variety of vascular  
toners. One can make compositions within the scope of my  
invention with minoxidil analogs or derivatives, or with  
other anti-alopecia agents, such as diphencyprone, which work  
in a similar way, by improving local blood flow to the  
affected hair bulbs. Because it has such a broad volume of  
10 use and scientific study, I prefer to use minoxidil. I thus  
use it as an example throughout this specification.

15 A vascular toner, if used to maintain healthy  
function of hair bulbs, must be delivered to the small blood  
vessels feeding the hair bulbs. I have thus found that the  
effectiveness of the vascular toner is greatly improved if it  
is topically applied along with a penetration enhancer. This  
allows the vascular toner to act locally.

20 The vascular toner must be carefully titrated  
against the penetration enhancer. For example, for a given  
concentration of minoxidil, one needs to use the penetration  
enhancer in the appropriate concentration. If a given  
penetration enhancer is used in a too high concentration, the  
minoxidil may penetrate through the skin and reach the  
systemic blood circulation. It can there, if present in

sufficient amount, cause side effects as seen by taking oral minoxidil. Thus, it is necessary to adjust the amounts of penetration enhancer and vascular toner, depending on the concentration and specific identity of the enhancer and the toner.

Adding a penetration enhancer to the vascular toner appears to fundamentally change the biological mechanism by which the vascular toner works. This is shown by the qualitatively different results seen between minoxidil and my compounds. The two products produce different types of hair, and for different time periods.

Minoxidil without a penetration enhancer (as available in ROGAINE™ topical minoxidil U.S.P.) produces a different kind of hair than does minoxidil used with a penetration enhancer. It is known in the art that topical minoxidil without a penetration enhancer (as is commercially available in ROGAINE (TM) topical minoxidil U.S.P., commercially available from Pharmacia & Upjohn Inc., Bridgewater, New Jersey) results in thin, baby-like, temporary hair, called "lanugo" hair. I have found that my compounds, by contrast, result in good, coarse, "terminal" hair, hair which is normal, permanent adult hair.

This indicates that minoxidil without and with penetration enhancer may act on different types of hair

bulbs, or produce different responses from the same hair  
bulbs. Minoxidil without enhancer is only weakly soluble in  
polar solvents. See supra. It thus has difficulty diffusing  
to the deeply located hair bulbs (roots) which are located  
just above the deep fat layer. Minoxidil without enhancer  
may thus affect only hair bulbs located close to the skin  
surface, or located in a less fatty skin layer, or hair bulbs  
most sensitive to changes in blood flow. Alternatively, it  
may affect the same hair bulbs, but with such weak or  
attenuated effect that the hair bulbs produce a different  
type of hair.

In contrast, my compounds produce normal, terminal  
hair. This indicates that my compounds act directly on the  
mature, adult hair bulbs responsible for terminal hair  
growth.

Further, it is known in the art that minoxidil  
users experience a sudden drop in hair thickness after about  
thirty months of usage. I thus have sought the time at which  
my compounds have a sudden drop in effectiveness.

Surprisingly, I have found that my compounds apparently do  
not lose effectiveness at all, even after using them for  
substantially greater than thirty months. This confirms that  
while my compounds appear to simply restore or preserve  
normal hair bulb function, the prior art compositions do not

restore normal hair bulb function, but actually provoke an abnormal function - the growth by an adult of baby like, temporary hair. That this function is abnormal is confirmed by its drop in effectiveness after thirty months; such a drop  
5 in efficacy indicates a "tolerance" acquired against the intervention, rather than the maintenance of a permanent, healthy state.

This indicates that the physiological mechanisms and biomedical pathways of the two preparations are  
10 different. Minoxidil alone, in the concentrations typically used, may actually temporarily alter a normal adult body function (causing the adult body to temporarily produce infant hair). In contrast, my invention simply maintains the normal function of the healthy adult body hair bulb, allowing  
15 it to continue to produce normal adult hair as long as the compound is used.

I have also found that the effect of the formulations depends on location of administration. Using the specific formulations disclosed here, I have observed  
20 decreases in hair loss, and a consequent statistically significant increase in the amount of healthy mature hair, after 4.0 - 4.5 months on the frontal scalp. On the crown and back of the head, by contrast, I have observed statistically significant results after 4.5 - 5.0 months.

The frontal scalp may react faster because it enjoys greater vascularization and blood flow than the other parts of the scalp.

5      Testosterone Blocker

My invention works with a variety of testosterone blockers. I prefer to use a blocker already approved for human use by the United States Food & Drug Administration, as these types of testosterone blockers, if used in pharmaceutical (as opposed to cosmetic) versions of my invention, do not need to undergo as lengthy and expensive a process to verify their safety and efficacy as used in pharmaceutical products. Examples include flutamide, cyproterone acetate, spironolactone, progesterone, or analogs or derivatives of any of these (e.g., 17-hydroxy-16-methylene- $\Delta^6$ -progesterone, 17 $\alpha$ -hydroxyprogesterone).

I have found several surprising things about testosterone blockers. First, they are not actually necessary for my invention to work; minoxidil alone is effective on 8% of patients, while the same amount of minoxidil administered with the proper amount of a penetration enhancer is effective on 35% of patients. Second, testosterone blockers added to such a mix are

synergistically beneficial, increasing the efficacy from 35% to 85% of patients.

One testosterone blocker is the anti alopecia compound cioteronel. Cioteronel is the common name for  
5 hexahydro-4-(5-methoxyheptyl)-2(1H)-pentalenone. It is also known, or is commercially available, as X-ANDRON™, CPC-10997, CYOCTOL™, and EXANDRON™. It is a clear, colorless oil, soluble in lipid and relatively non-polar solvents. Its preparation is disclosed in Kasha, W.J., PCT Int'l Patent Application  
10 83/04,019 (1983), 101 Chem. Abstr. 23037k (1984). Its use is disclosed in United States Letter Patent No. 4,689,345. Its inhibition of DHT binding in vitro is disclosed in Rec. Adv. Chemotherapy (Proc. 14<sup>th</sup> Int'l Congr. Chemotherapy Antimicrob., Sect. 1) at 261-70 and 273-74  
15 (Univ. Tokyo Press, 1985). Its cutaneous metabolism and clinical pharmacokinetics is disclosed in de Zeeuw et al., 7 Pharm. Res. 638 (1990), Weichers et al., 65 Int. J. Pharm. 77 (1990).

Another testosterone blocker is progesterone,  
20 pregn-4-ene-3, 20-dione (commercially available as CORLUTINA™, CORLUVITE™, CYCLOGETS™, GESTIRON™, GESTONE™, LIPOLUTIN™, LUTOCYCLIN M™, PROGESTIN™, CP progesterone powder, etc . . .). Progesterone is insoluble in water and soluble in alcohol, acetone, dioxane, and concentrated



sulfuric acid. It is sparingly soluble in vegetable oils.  
Its isolation, structure and biological activity is described  
at length in Bardin et al. (eds.), Progesterone and  
Progestins (Raven Press, New York 1982). I prefer to use  
5 progesterone as the sole testosterone blocker.

### Carrier Vehicles

The penetration enhancer and the vascular toner or  
testosterone blocker, or both, may be mixed with a carrier  
10 vehicle. You can use a variety of vehicles to make my  
invention. The vehicle is simply a cosmetically safe,  
medically safe solvent for the active ingredients. The  
vehicle should not adversely and significantly chemically  
react with the active ingredients.

15 For example, propylene glycol, water and isopropyl  
alcohol may be used as vehicles. These may be used alone or  
in combination.

The vehicle can optionally provide functions in  
addition to simply dissolving the active ingredients. For  
20 example, one can use a moisturizing vehicle, or a vehicle  
containing sunscreen. For a moisturizing or moisture  
retaining vehicle, one can use a vehicle made from a  
combination of (ranked in order of quantity used) water,  
mineral oil, petrolatum, lanolin, sorbitol solution, stearic

acid, lanolin alcohol, cetyl alcohol, glyceryl stearate /  
PEG-100 stearate, triethanolamine, dimethicone, propylene  
glycol, tri(PPG-3 myristyl ether) citrate, disodium EDTA,  
methylparaben, ethylparaben, propylparaben, fragrance,  
5 xanthan gum, butylparaben, and methyldibromo glutaronitrile.

It may be desirable to use a vehicle containing one  
or more sunscreens. This is because my preparations are used  
on the tops of balding scalps. Balding scalps are often  
largely unprotected from sun damage, as the user may not wear  
10 headgear and the balding scalp lacks the sun shielding dense  
hair layer present on a healthy scalp. Adding sunscreen thus  
can protect the scalp from possible sun damage. Sunscreens,  
and vehicles containing sunscreen compounds, are widely known  
in the art. See, e.g., United States Letter Patent No.  
15 4,522,807.

Other cosmetic vehicles are widely known in the  
art. I prefer to use VEHICLE/N<sup>TM</sup> as the vehicle. I prefer to  
use VEHICLE/N (TM) because it has a cosmetically attractive  
"feel" to the user. Vehicle/N (TM) is commercially available  
20 from the Neutrogena Dermatologics division of Johnson &  
Johnson, Inc., New Brunswick, New Jersey. It is currently  
available in two formulations, regular and mild. They are  
both versatile liquid vehicles for extemporaneous compounding  
of topical drugs. Both formulations solublize selected

dermatological agents and provide astringent and drying actions.

5 The VEHICLE/N (TM) ingredients are SD alcohol 40 (45%), purified water (<45%), laureth-4 (>4%), isopropyl alcohol (4%) and propylene glycol (<4%). The VEHICLE/N (TM) mild ingredients are purified water (>37.5%), SD alcohol-40 (37.5%), isopropyl alcohol (5%) and laureth-4 (<5%). To compound with VEHICLE/N, add the appropriate quantity of active ingredient to yield the intended concentration.

10 VEHICLE/N (TM) is available as 50 mL of vehicle in a plastic bottle with applicator top. The bottle is filled only to 3/4 capacity, to ensure proper mixing. For 50 mL of VEHICLE/N, use the following amounts:

<b>Desired Concentration</b>	<b>0.1%</b>	<b>0.2%</b>	<b>0.5%</b>	<b>1.0%</b>
Bulk Active	50 mg	100 mg	250 mg	500 mg
Tablets			1x250mg	4x150 mg 1.2% soln
<b>Desired Concentration</b>	<b>2.0%</b>	<b>3.0%</b>	<b>4.0%</b>	<b>5.0%</b>
Bulk Active	1.0 gm	1.5 gm	2.0 gm	2.5 gm

15 For fastest dissolution, when tablets are used, crush them to a powder and then add the powder to the vehicle. When capsules are used, add the capsule contents only to the vehicle, and discard the capsule shell. Shake the mixture

gently. Most capsule contents and bulk active ingredients will dissolve within minutes, though some may take longer.

VEHICLE/N™ is available in a bottle with an APPLIDERM (TM) applicator top. The APPLIDERM (TM) applicator unit automatically filters the compounded mixture and provides a convenient, spill-proof, self-contained unit for topical application. To use the APPLIDERM (TM) applicator unit, push the applicator firmly into the bottle using the white cap as a holder. Screw the cap all the way down to seat the applicator. Shake well. If tablets are dissolved in the vehicle, then the user should be instructed to allow the solution to stand overnight and to shake vigorously before the first use. VEHICLE/N (TM) should not be used near fire or open flame due to alcohol content. Both VEHICLE/N (TM) and VEHICLE/N (TM) mild contain substantial alcohol and are not suitable for use in acute dermatoses. Stinging may be noted if used on irritated or abraded skin. Avoid contact with eyes or eyelids. If the product accidentally comes in contact with eyes, rinse thoroughly with water and contact physician. Keep out of reach of children. VEHICLE/N (TM) and VEHICLE/N (TM) mild are contraindicated in persons who have shown hypersensitivity to any of the listed ingredients.

### Preferred Formulations

Given a constant amount of testosterone blocker or vascular toner, I have found that lower concentrations of penetration enhancer can decrease the efficacy of the final formulation, while higher concentrations of penetration enhancer increase the risk of adverse side effects due to systemic penetration of the other active ingredient(s).

Similarly, you may use different testosterone blockers for the same effect, and may use more or less of it. Using more testosterone blocker allows one to use relatively less penetration enhancer, or a weaker enhancer. Titration of the two components against one another is a conventional technique well known in the art of pharmaceutical and cosmetics formulation. Such techniques are already used to titrate formulations for the wide variety of trans-dermal drugs and cosmetics currently available.

For example, in a four ounce quantity of liquid containing 5 drops of trimethyl acetate, I prefer to use one percent (by volume) of soluble progesterone (U.S.P.).

A preferred formulation is:

Minoxidil	1.0 gm bulk powder
Soluble progesterone (U.S.P.)	0.5 gm
Trimethyl acetate	5 drops
Vehicle N (TM)	50 mL

The following preparation is acceptable, and within the scope of the claims, but I do not prefer it:

Minoxidil	1.0 gm bulk powder
Soluble progesterone (U.S.P.)	0.5 gm
Methyl acetate	5 drops
Vehicle N-(TM)	50 mL

5

Alternatively, an ethyl alcohol - water - propylene glycol solution may be used as the diluents and vehicle. For 100 mL of this formulation, use:

ethyl alcohol 95%	75.5 cc
purified water	18.5 cc
propylene glycol	6.0 cc
progesterone	1.5 gm
minoxidil	2.0 - 5.0 gm
methyl acetate	5.0 gtts

10

These are my preferred formulations. These may be varied as desired, but it is necessary to watch for unwanted side effects possibly due to unwanted systemic penetration of the active ingredient(s). For example, minoxidil is pharmaceutically and cosmetically effective topically at

anywhere from about 0.01 grams to about 50 grams per four  
ounces, depending on the frequency of topical administration.  
Testosterone blockers are also pharmaceutically and  
cosmetically effective topically at anywhere from about 0.01  
5 grams to about 50 grams per four ounces, depending on the  
frequency of topical administration. With the higher  
concentrations, however, increasing the amount of penetration  
enhancer creates a greater risk of adverse side effects.

10 Summary

I have discussed several different specific  
formulas. I have found these most useful. One can, however,  
vary the constituents to achieve the same effect without  
having a substantially different product. For example, one  
15 can use a different testosterone blocker, or a weaker  
penetration enhancer in a higher concentration. Thus, the  
legal scope of my patent is not limited to the specific  
examples I discuss herein; rather, the legal coverage of this  
patent is defined by the appended claims and their  
20 equivalents.